UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/506,988	02/18/00	TANG	[illegible]

HM12/0308

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EXAMINER	
SEAMAN, D	

ART UNIT	PAPER NUMBER
1625	13

DATE MAILED: 03/08/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/506,988	TANG ET AL.	
	Examiner	Art Unit	
	D. Margaret Seaman	1625	

-- The MAILING DATE of this communication app ars on the cover she t with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. This application was filed 18 February 2000 and claims priority to 60/120,835, filed 19 February 1999. Claims 1-12 remain before the examiner.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-12 remain rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Critical or essential method parameters and core structure which is necessary to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976) (e.g. critical reaction parameters); and. *Ex Parte Bhide* (Bd Pat. App. & Int.) 42 USPQ2d 1441 (e.g. critical core structure). Additionally, the specification fails to adequately describe the making and use of any "transition-state isostere" within the scope of the presently claimed invention.

The disclosed and claimed invention is drawn to inhibiting protease (aspartic acid protease) which leads to the treatment of HIV. Additionally, the invention broadly

encompasses the treatment of HIV by using any compound having two or more transition-state isosteres.

The claims are not enabled for the following reasons:

a. The prior art demonstrates the criticality of the choice and amount of compound and the conditions effective to inhibit theHIV-1 protease. In order to incorporate compounds that are divergent in size and properties and in view of the unpredictability and stereospecificity of binding to the protease. Claim parameters that are critical to the practice of an invention which are not included in the claims, renders the resulting claims nonenabled by the disclosure. *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

b. The claims broadly encompass the incorporation of an unlimited number of types of compounds (e.g. differing in structure, function, physicochemical properties etc.) into a pharmaceutical composition and specifically the formation of pharmaceutical compositions containing different therapeutic agents that vary in size, physical and chemical properties, for in vivo delivery.

The specification fails to provide enablement for the scope of different compounds to be loaded into a pharmaceutical composition. Additionally, no guidance is provided on how to incorporate large and structurally diverse therapeutic compounds into compositions useful for pharmaceutical delivery. The size, shape, conformation which is dependent upon the therapeutic agent is considered critical to the practice of the presently claimed method(s) since such parameters have been

demonstrated to be critical for obtaining efficacy (e.g. drug delivery). See *Ex Parte Bhide* (Bd Pat. App. & Int.) 42 USPQ2d 1441 (e.g. critical core structure necessary for biological activity must be present in the claimed invention.).

The prior art clearly demonstrates the criticality of the choice of compound, the amount of compound and the conditions (e.g. pH, temperature, administration time) in order to achieve effective inhibition of protease) to incorporate compounds that are large in size and/or which differ in physical/chemical properties. This criticality results from the unpredictability of the compound in binding to the protease, which differs from compound to compound, and which are stereospecific with respect to the compound.

Further, the presently claimed invention broadly discloses and claims the administration (e.g. pharmaceutics to be administered) of bioactive/therapeutic compounds for in vivo therapeutic delivery (e.g. cytokines). The claimed invention is not enabled for the scope of compounds and modes of administration (e.g. oral, internal, parenteral) of these compounds.

The pharmaceutical use of bioactive/therapeutic compounds encompasses a broad range of peptides, proteins, steroids etc. that vary in structure and properties which include, but are not limited to, primary/secondary & tertiary structure, solubility, hydrophobicity, specificity, in vivo activity, susceptibility to enzymatic degradation and immunogenicity.

Claims drawn to pharmaceuticals and in vivo methods of use (e.g. treatment) generally require supporting data because of the unpredictability in biological responses to therapeutic treatments. In vivo utility necessarily involves unpredictability with respect to physiological activity of an asserted process in humans. See discussion in Ex parte Kranz, 19 USPQ2d 1216,1218-1219 (6/90). For example, drug delivery to the targeted area must survive the acidic environment of the stomach if administered orally. Additionally, the delivery of the drug across necessary cell surfaces in amounts needed to be efficacious, but not lethal to the organism, necessitates sensitive testing in order to adequately determine the proper human dosage. For the difficulty and unpredictability of formulating pharmaceutically effective compositions which comprise active ingredients of variable properties is known in the art. Avoiding enzymatic degradation upon delivery (e.g. oral, parenteral etc.) and successful tissue targeting are just some of the difficulties faced when designing pharmaceutical dosage form.

In the present case, to demonstrate efficacy, no evidence is provided. Accordingly, absent additional evidence to the contrary, it would constitute undue experimentation for the skilled artisan to practice the presently claimed invention.

The only compound that is enabled by the instant specification is the UIC-98-056 compound.

The rejection of claims 1-12 under 35 USC §112, first paragraph, as stated above and in paper #7, is upheld.

Conclusion

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 703-308-4528. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms
March 7, 2001